

## REMARKS

Claim 4 has been amended herein. Claims 6, 7, and 12-21 were canceled in Applicants' earlier response. Claims 1-5 and 8-11 remain in the case.

This amendment is necessary and was not entered earlier because the Office, in the Advisory Office Action, indicated that Claim 4 as amended in Applicants' earlier response was rejected, but failed to provide any reason why Claim 4 as amended was rejected.

On March 23, 2005, a telephone interview was held between Applicants' undersigned counsel and Examiner Monshipouri. During that conversation, Applicants' counsel pointed out the Claim 7, a method claim now canceled from the case, was not subject to any prior art rejections. Claim 7 was subject to a rejection under §112, first paragraph, but that rejection was addressed by amending the base claim. The Advisory Office Action indicates that Applicants' prior response overcame the rejections under §112. See box 5 of the Advisory Office Action.

In the Final Office Action, Claims 1-5, 8-9, and 11 were rejected under §102(b) in view of Pupo et al. **Claim 7 was not made subject to this prior art rejection.** As noted in Applicants' prior response, Claim 4 was therefore amended to include the subject matter of Claim 7. By inserting the subject matter of Claim 7 (a claim not subject to this rejection) into Claim 4, coupled with the Office's indication that the rejection under §112 has been overcome, Applicants respectfully submit that there is no substantive basis now of record for the continued rejection of Claim 4 and the claims dependent thereon.

Claim 4 does, however, refer to Claim 1, which currently stands rejected under §102(b) in view of Pupo et al. Therefore, this Supplemental Amendment After Final is being submitted to incorporate into Claim 4 the subject matter of Claim 1 that was previously only incorporated by reference. **Note that the scope of Claim 4 remains unchanged from Applicants' prior response.** The amendment does not alter the scope of Claim 4 in any fashion, nor does it introduce new matters for search or consideration. The amendment does not touch the substantive merit of Claim 4 in any

fashion. Therefore, Applicants respectfully request that this Supplemental Response After Final be entered and considered..

As applied to Claims 4, 5, and 8-10, the §102(b) rejection in view of Pupo et al. is believed to have been overcome by appropriate amendment to Claim 4. Again, to note with particularity the changes made to Claim 4, Claim 4 includes the subject matter of earlier Claim 7. Claim 7 **was not** made subject to this rejection. Therefore, by incorporating the subject matter of Claim 7 into Claim 4, Claim 4 is likewise not subject to this rejection. Claim 4 also now includes an explicit recitation of the construct to be used in the method.

Applicants also reiterate their prior traversal of this rejection as applied to Claims 1, 2, and 11. This rejection is respectfully traversed as applied to Claims 1, 2, and 11. The Examiner's characterization of the Pupo et al. reference is not logically sound. The Examiner states (at the top of page 6 of the Final Office Action) that Pupo et al. teach that "most of the insoluble [*sic*] SKC fraction could be washed off with buffers, but the reference fails to say that all of said insoluble [*sic*] fraction was washed off in its entirety." (Emphasis in the original.) As a factual matter, Pupo et al. **never** said the SKC activity present in the "insoluble fraction" was itself insoluble. Pupo et al. wrote that "the low amount of SKC **in** the insoluble fraction" was caused by contamination with "soluble SKC." See Pupo et al., 1122, left-hand column, first paragraph. There is no ambiguity in this statement. Pupo et al.'s "insoluble fraction" **did not** contain "insoluble" SKC as alleged by the Office. Pupo et al.'s "insoluble fraction" was contaminated with "soluble SKC." This soluble contamination could be largely removed by washing with PBS.

The Examiner's conclusion that the SKC activity remaining in the insoluble fraction is therefore "insoluble" is not supported by the clear language of the Pupo et al. reference. Pupo et al. does not say that the SKC activity found in the "insoluble fraction" is insoluble. Pupo et al. clearly state that the SKC activity is a **contamination from the soluble fraction**. Pupo et al. go on to state that most of it was removed by washing with PBS. The remaining SKC activity could have remained there for any

number of reasons **totally unrelated to solubility**, including adsorption to disrupted cell fragments. In other words, had Pupo et al. been a little more careful in separating the soluble fraction from the insoluble fraction, the contamination would not have happened in the first place, and Pupo et al.'s insoluble fraction would have been devoid of SKC activity.

Lastly, the Office states that "Pupo's intention in expressing its streptokinase is, in fact, irrelevant" (Office Action, page 5). Applicants respectfully disagree. Pupo et al. teach a method of expressing **soluble** SKC and state that an "insoluble fraction" was found to contain a small amount of SKC activity. But the authors go on to state that the SKC activity in the insoluble fraction was due to contamination of this fraction with **soluble** SKC (p. 1122, left hand column, first paragraph). Pupo et al. go on in that same paragraph to state that "most of this protein could be removed by washing several time with PBS." Thus, Pupo et al. clearly indicate that the SKC activity found in the insoluble fraction was an accidental contamination of the insoluble fraction with soluble SKC activity.

Thus, Pupo et al. cannot be considered an anticipatory reference because a valid anticipatory reference must **teach**. Pupo et al. do not teach anything regarding making insoluble and enzymatically active streptokinase. They teach only that one should be careful in separating the soluble fractions from the insoluble fractions so as not to cause cross-contamination. For instance, in *In re Wilder*, 429 F.2d 447, 166 USPQ 545 (C.C.P.A. 1970). A prior art reference:

may yet be held **not** to legally anticipate the claimed subject matter if it is found not to be sufficiently enabling, in other words, if it does not place the subject matter of the claims within the possession of the public.

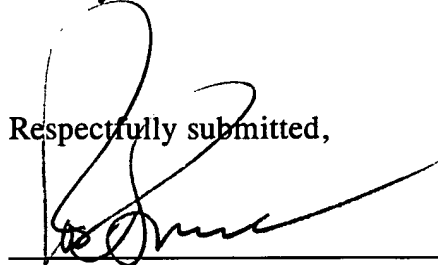
Here, Pupo et al. do not enable the public to fabricate insoluble SKC in the form of an enzymatically active inclusion body. Pupo et al. merely show in Fig. 2, lane 6 that the insoluble cell fragment may be contaminated by **soluble** SKC.

Therefore, the rejection of Claims 1-5, 8-9, and 11 Under 35 USC §102(b) is untenable. Withdrawal of the same is respectfully requested.

### CONCLUSION

In light of the above amendments and remarks, Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,



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